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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,884	04/07/1999	HAROLD J. WANEBO	58463/JPW/EM	6824

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EXAMINER
ANDERSON, JAMES D

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
12/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/287,884	WANEBO ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-33 and 42-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *20-29,31-33 and 42-54* is/are allowed.

6)☒ Claim(s) *30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 8/18/2008, are acknowledged and entered. Claims 42-54 have been newly added by Applicant. Claims 20-33 and 42-54 are pending and under examination.

Declaration under 37 C.F.R. 1.132

The Declaration of Dr. Harold Wanebo has been received and entered into the record. However, the Declaration has not been considered because it is incomplete. The Examiner notes that pages 3 and 4 of the Declaration are missing and as such, it is not clear what experiments resulted in the data presented in Exhibits B-G. The Examiner has relied on the discussion of the data presented in Exhibits B-G as presented in Applicant's remarks at pages 14-17 with respect to the unexpected results of the claimed combinations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 20, 25, and 31 under 35 U.S.C. 103 as being unpatentable over Jayadev et al. in view of Mycek et al., is **withdrawn** in light of Applicants' amendments and arguments. Specifically, limitation of the claims to the treatment of head and neck tumors with a combination of paclitaxel and C6-ceramide are considered unobvious over the cited prior art in light of Applicant's demonstration of unexpected superiority of such treatment versus administration of either agent alone.

The rejection of claims 20-29 and 31-33 under 35 U.S.C. 103 as being unpatentable over Spencer et al. in view of Cai et al., is **withdrawn** in light of Applicants' amendments and arguments. Specifically, limitation of the claims to the treatment of head and neck tumors with a combination of paclitaxel and C6-ceramide are considered unobvious over the cited prior art in light of Applicant's demonstration of unexpected superiority of such treatment versus administration of either agent alone.

Claim 30 is again rejected under 35 U.S.C. § 103(a) as being unpatentable over **Jayadev *et al.*** (J. Biol. Chem., 1995, vol. 270, pages 2047-2052) in view of **Mycek *et al.*** (Lippincott's Illustrated Review: Pharmacology 2nd Edition, 1997, pages 376 and 390-392).

Jayadev *et al.* teach that C_6-ceramide causes apoptosis in Molt-4 leukemia cells through significant G_0/G_1 arrest (Abstract). The reference also teaches that the effects of C_6-ceramide on cell cycle arrest are a generalized phenomenon, not restricted to the Molt-4 cell line (page 2049).

Mycek *et al.* teach that paclitaxel has shown good activity against advanced ovarian cancer and metastatic breast cancer and has shown further favorable results in small-cell lung cancer, squamous-cell carcinoma of the head and neck, and "several other cancers". In addition, Mycek *et al.* teach that combination therapy of paclitaxel with other anticancer drugs is being evaluated.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to formulate a pharmaceutical composition comprising paclitaxel, C_6-ceramide, and a pharmaceutical carrier. One would have been motivated to do so because each of the therapeutics have been individually taught in the prior art to be successful at treating cancer, and further, Mycek *et al.* motivates

combination therapy for the treatment of cancer using paclitaxel and a second therapeutic agent. Moreover, the instant situation is amenable to the type of analysis set forth in *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant claims, one of ordinary skill in the art would have been imbued with at least a reasonable expectation that a composition comprising C_6-ceramide in combination with paclitaxel as taught in Jayadev *et al.* in view of the teachings of Mycek *et al.*, would be effective for the treatment of cancer.

Accordingly, the composition of claim 30 is deemed properly rejected under 35 U.S.C. § 103 as being obvious over Jayadev *et al.* in view of Mycek *et al.* Applicant's demonstration of unexpected results is not commensurate in scope with claimed pharmaceutical composition, which could reasonably be used to treat other cancers, such as breast cancer.

Claim 30 is again rejected under 35 U.S.C. § 103(a) as being unpatentable over **Spencer *et al.*** (Drugs, 1994, vol. 48, pages 794-847) in view of **Cai *et al.*** (J. Biol. Chem., 1997, vol. 272, pages 6918-6926).

Spencer *et al.* teach that paclitaxel has demonstrated broad-spectrum anticancer activity, including activity in treating the specific cancers recited in the instant claims (Table 1). The reference also teaches combination therapy comprising paclitaxel and several other anticancer agents, including cisplatin, cyclophosphamide, doxorubicin, hydroxyurea and dexamethasone (pages 798-799, 805-806 and 821-826). Such combinations are often synergistic as discussed *supra*.

Cai *et al.* teach that C_6-ceramide induces apoptosis in both TNF-sensitive and TNF-resistant breast cancer cells (pages 6922-6923; Figure 5).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to formulate a pharmaceutical composition comprising paclitaxel, C_6-ceramide, and a pharmaceutical carrier. One would have been motivated to do so because each of the therapeutics have been individually taught in the prior art to be successful at treating cancer, and further, Spencer *et al.* motivates

combination therapy for the treatment of cancer using paclitaxel and a second therapeutic agent. Moreover, the instant situation is amenable to the type of analysis set forth in *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant claims, one of ordinary skill in the art would have been imbued with at least a reasonable expectation that a composition comprising C_6-ceramide in combination with paclitaxel as taught in Spencer *et al.* in view of the teachings of Cai *et al.*, would be effective for the treatment of cancer.

Accordingly, the composition of claim 30 is deemed properly rejected under 35 U.S.C. § 103 as being obvious over Spencer *et al.* in view of Cai *et al.* Applicant's demonstration of unexpected results is not commensurate in scope with claimed pharmaceutical composition, which could reasonably be used to treat other cancers, such as breast cancer.

Allowable Subject Matter

Claims 20-29, 31-33, and 42-54 are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614